

**What Is Claimed is:**

1. A method for detecting whether a subject is likely to have a colon neoplasia comprising:
  - 5 a) obtaining a biological sample from said subject;
  - b) detecting one or more polypeptides selected from among: one or more ColoUp1 polypeptides and one or more ColoUp2 polypeptides, wherein the presence of said one or more polypeptides is indicative of colon neoplasia.
- 10 2. The method of claim 1, wherein the ColoUp1 polypeptide is encoded by a nucleic acid sequence that is at least 95% identical to the nucleic acid sequence of SEQ ID No: 4.
3. The method of claim 1, wherein the ColoUp1 polypeptide is encoded by a nucleic acid sequence that is at least 98-99 % identical to the nucleic acid sequence of  
15 SEQ ID No: 4.
4. The method of claim 1, wherein the ColoUp1 polypeptide is encoded by SEQ ID No: 4.
5. The method of claim 1, wherein the ColoUp2 polypeptide is encoded by a nucleic acid sequence that is at least 95% identical to the nucleic acid sequence of  
20 SEQ ID No: 5.
6. The method of claim 1, wherein the ColoUp2 polypeptide is encoded by a nucleic acid sequence that is at least 98-99% identical to the nucleic acid sequence of SEQ ID No: 5.
7. The method of claim 1, wherein the ColoUp2 polypeptide is encoded by SEQ  
25 ID No: 5.

8. The method of claim 1, wherein the ColoUp1 polypeptide is encoded by a nucleic acid sequence that hybridizes under stringent conditions to a nucleic acid sequence of SEQ ID No: 4.
- 5 9. The method of claim 1, wherein the ColoUp2 polypeptide is encoded by a nucleic acid sequence that hybridizes under stringent conditions to a nucleic acid sequence of SEQ ID No: 5.
- 10 10. The method of claim 2, wherein the ColoUp1 polypeptide is encoded a nucleic acid encoding a polypeptide comprising an amino acid sequence that is at least 95% identical to the amino acid sequence as set forth in any one of SEQ ID No: 1, SEQ ID No: 2 and SEQ ID No: 13.
11. The method of claim 5, wherein the ColoUp2 polypeptide is encoded a nucleic acid encoding a polypeptide comprising an amino acid sequence that is at least 95% identical to the amino acid sequence as set forth in any one of SEQ ID No: 3 and SEQ ID No:14.
- 15 12. The method of claim 1, wherein said biological sample is selected from the group consisting of whole blood or a fraction thereof.
13. The method of claim 1, wherein said biological sample is selected from the group consisting of urine or stool samples.
14. The method of claim 1, wherein said biological sample is a blood sample.
- 20 15. The method of claim 14, wherein said blood sample is fractionated to obtain blood serum and/or blood plasma.
16. The method of claim 15, wherein said biological sample is enriched for ColoUp1 or ColoUp2.
17. The method of claim 1, wherein the polypeptide is detected by an assay.
- 25 18. The method of claim 17, wherein said assay employs an antibody.

19. The method of claim 18, where said assay is selected from the group consisting of an immunoprecipitation assay, a Western blot, a radioimmunoassays and an enzyme-linked immunosorbent assay (ELISA).
- 5 20. The method of claim 18, wherein said assay comprises contacting the biological sample with an antibody that interacts with ColoUp1 polypeptide or the ColoUp2 polypeptide.
21. The method of claim 20, wherein the antibody interacts with an epitope selected from among: an epitope on SEQ ID No: 1 and an epitope on SEQ ID No: 2
- 10 22. The method of claim 20, wherein the antibody interacts with an epitope selected from among: an epitope on SEQ ID No: 3 and an epitope on SEQ ID No: 14.
23. The method of claim 20, wherein the antibody is detectably labeled.
24. The method of claim 24, wherein the label is selected from the group consisting of an enzyme, a fluorescent substance, a chemiluminescent substance, a chromophore, a radioactive isotope and a complexing agent.
- 15 25. A purified antibody that interacts with an epitope selected from among: an epitope on SEQ ID No: 1 and an epitope on SEQ ID No: 2.
26. A purified antibody that interacts with an epitope selected from among: an epitope on SEQ ID No: 3 and an epitope on SEQ ID No: 14.
27. The antibody of claim 25, wherein the antibody is a monoclonal antibody.
- 20 28. The antibody of claim 26, wherein the antibody is a monoclonal antibody.
29. A hybridoma cell line that produces the antibody of claim 27.
30. A hybridoma cell line that produces the antibody of claim 27.

31. The method of claim 1, comprising detecting the amount of the at least one ColoUp1 polypeptide and/or the at least one ColoUp2 polypeptide in the biological sample.

5 32. The method of claim 31, wherein the amount of the at least one ColoUp1 polypeptide and/or the at least one ColoUp2 polypeptide in the biological sample is compared to a predetermined standard.

33. The method of claim 31, wherein the amount of the at least one ColoUp1 polypeptide and/or the at least one ColoUp2 polypeptide in the biological sample is compared to a predetermined standard.

10 34. The method of claim 31, wherein the amount of the at least one ColoUp1 polypeptide and/or the at least one ColoUp2 polypeptide in the biological sample is compared to the subject's historical baseline.

15 35. The method of claim 1, wherein the presence of the at least one ColoUp1 and/or at least one ColoUp 2 polypeptide is indicative that the subject is likely to develop colon neoplasia.

36. The method of claim 1, wherein the presence of the at least one ColoUp1 and/or at least one ColoUp 2 polypeptide is indicative that the subject is likely to harbor a colon adenoma or a colon cancer.

20 37. The method of claim 1, wherein the presence of the at least one ColoUp1 and/or at least one ColoUp 2 polypeptide aids in determining the therapeutic protocol to be administered to the subject having a colon neoplasia.

38. The method of claim 37, wherein the subject was not previously diagnosed with colon cancer.

25 39. The method of claim 37, wherein the subject has previously received or is currently receiving a therapy for colon cancer, wherein the presence of the at least one ColoUp1 polypeptide and/or at least one ColoUp 2 polypeptide indicates that the subject is likely to have a relapse or a persistent or progressive colon cancer.

40. The method of claim 1, wherein the colon neoplasia is a colon adenoma.
41. The method of claim 1, wherein the colon neoplasia is selected from among: a colon cancer and a metastatic colon cancer.
42. The method of claim 1, comprising detecting at least one ColoUp1 polypeptide and at least one ColoUp2 polypeptide in the biological sample.
43. A kit for detecting colon neoplasia in a biological sample, comprising:
- a) an antibody which interacts with an epitope of ColoUp1 or ColoUp2; and
  - b) instructions for use.
44. A kit for detecting colon neoplasia in a biological sample, comprising:
- a) an antibody which interacts with a polypeptide having an amino acid sequence as set forth in any one of SEQ ID Nos: 1-3; and
  - b) a container.
45. The kit of claim 44, wherein said antibody is detectably labeled.
46. The kit of claim 45, wherein said label is selected from the group consisting of an enzyme, a fluorescent substance, a chemiluminescent substance, a chromophore, a radioactive isotope and a complexing agent..
47. A recombinant nucleic acid comprising a nucleic acid sequence that is at least 95% identical to a nucleic acid sequence of SEQ ID No: 5, or a complement thereof.
48. The recombinant nucleic acid of claim 47, wherein the recombinant nucleic acid comprises a nucleic acid sequence that is at least 99.5% identical to a nucleic acid sequence of SEQ ID No: 5, or a complement thereof.
49. The recombinant nucleic acid of claim 47, wherein the recombinant nucleic acid comprises a nucleic acid sequence that is identical to the nucleic acid of SEQ ID No: 5 or a complement thereof.

50. A recombinant nucleic acid comprising a nucleic acid sequence that encodes a polypeptide that is at least 95% identical to a polypeptide selected from the group consisting of SEQ ID Nos: 3 and 14, or a complement thereof.

5 51. The recombinant nucleic acid of claim 50, wherein the recombinant nucleic acid comprises a nucleic acid sequence that encodes a polypeptide that is at least 99.5% identical to a polypeptide selected from the group consisting of SEQ ID Nos: 3 and 14, or a complement thereof.

10 52. The recombinant nucleic acid of claim 50, wherein the recombinant nucleic acid comprises a nucleic acid sequence that encodes a polypeptide that is identical to a polypeptide selected from the group consisting of SEQ ID Nos: 3 and 14, or a complement thereof.

53. An expression construct comprising the recombinant nucleic acid of claim 50.

54. A vector comprising the expression construct of claim 53.

55. A cell comprising the expression construct of claim 53.

15 56. A cell of claim 55, wherein the cell is selected from the group consisting of: a bacterial cell and a eukaryotic cell.

57. A method of preparing a ColoUp2 polypeptide comprising,

(a) obtaining a cell of claim 55;

20 (b) culturing the cell under conditions that promote production of the polypeptide encoded by the recombinant nucleic acid;

(c) obtaining a cellular fraction that comprises the polypeptide encoded by the recombinant nucleic acid.

58. A method of claim 57, further comprising purifying the cellular fraction of (c) to obtain a substantially pure ColoUp2 polypeptide.

59. A recombinant polypeptide comprising an amino acid sequence that is at least 95% identical to a sequence selected from the group consisting of SEQ ID Nos: 3 and 14.

5 60. The recombinant polypeptide of claim 59, wherein the recombinant polypeptide comprises an amino acid sequence that is at least 99.5% identical to a sequence selected from the group consisting of SEQ ID Nos: 3 and 14.

61. The recombinant polypeptide of claim 59, wherein the recombinant polypeptide comprises an amino acid sequence that is identical to a sequence selected from the group consisting of SEQ ID Nos: 3 and 14.

10 62. The recombinant polypeptide of claim 59, wherein the recombinant polypeptide further comprises an epitope tag that facilitates detection of the recombinant polypeptide with an antibody.

63. A purified polypeptide comprising an amino acid sequence that is at least 95% identical to a sequence selected from the group consisting of SEQ ID Nos: 3 and 14.

15 64. The purified polypeptide of claim 63, wherein the purified polypeptide comprises an amino acid sequence that is at least 99.5% identical to a sequence selected from the group consisting of SEQ ID Nos: 3 and 14.

20 65. The purified polypeptide of claim 63, wherein the purified polypeptide comprises an amino acid sequence that is identical to a sequence selected from the group consisting of SEQ ID Nos: 3 and 14.

66. A fusion protein comprising a first polypeptide domain and a second polypeptide domain, wherein the first polypeptide domain consists of an amino acid sequence that is at least 95% identical to an amino acid sequence selected from the group consisting of: SEQ ID No. 3 and SEQ ID No. 14.

25 67. The fusion protein of claim 66, wherein the second polypeptide domain is a domain selected from the group consisting of: a detection domain, a purification domain and an antigenic domain.

68. An antibody that binds specifically to a ColoUp2 polypeptide of claim 63.

69. The antibody of claim 68, wherein the antibody binds the ColoUp2 polypeptide with a dissociation constant of less than  $10^{-6}$ M.

70. The antibody of claim 68, wherein the antibody is a monoclonal antibody.

5 71. The antibody of claim 68, wherein the antibody is effective for binding specifically to the ColoUp2 polypeptide in a blood sample.

72. The antibody of claim 68, wherein the antibody is effective for binding specifically to the ColoUp2 polypeptide in a sample comprising cells from a colon neoplasia.

10 73. A method for generating a monoclonal antibody that binds specifically to a ColoUp2 polypeptide of claim 63, the method comprising:

(a) administering to a mouse an amount of an immunogenic composition comprising the ColoUp2 polypeptide effective to stimulate a detectable immune response;

15 (b) obtaining antibody-producing cells from the mouse and fusing the antibody-producing cells with myeloma cells to obtain antibody-producing hybridomas;

20 (c) testing the antibody-producing hybridomas to identify a preferred hybridoma, wherein the preferred hybridoma is a hybridoma that produces a monoclonal antibody that binds specifically to the ColoUp2 polypeptide;

(d) culturing the preferred hybridoma cell culture that produces the monoclonal antibody that binds specifically to the Co; and

25 (e) obtaining the monoclonal antibody that binds specifically to the ColoUp2 polypeptide from the cell culture.



74. The method of claim 73, wherein testing the antibody-producing hybridomas comprises testing whether the antibody-producing hybridomas produce an antibody that binds to the ColoUp2 polypeptide in an assay selected from the group consisting of: an enzyme-linked immunosorbent assay, a Bia-core assay and an immunoprecipitation assay.

75. A method for detecting whether a subject is likely to have a colon neoplasia comprising:

- a) obtaining a biological sample from said subject;
- b) detecting one or more polypeptides selected from among: one or more secreted ColoUp1 polypeptides and one or more secreted ColoUp2 polypeptides, wherein the presence of said at least one polypeptide is indicative of colon neoplasia.

76. The method of claim 75, wherein the secreted ColoUp2 polypeptide is selected from among:

- a) a secreted polypeptide produced by the expression of a nucleic acid that is at least 95% identical to the amino acid sequence of SEQ ID No: 5;
- b) a secreted polypeptide produced by the expression of a nucleic acid that is a naturally occurring variant of SEQ ID No: 5;
- c) a secreted polypeptide produced by the expression of a nucleic acid that hybridizes under stringent conditions to a nucleic acid sequence of SEQ ID No: 5;
- d) a secreted polypeptide having a sequence that is at least 95% identical to the amino acid sequence of SEQ ID No: 3; and
- e) a secreted polypeptide having a sequence that is at least 95% identical to the amino acid sequence of SEQ ID No: 21.

77. The method of claim 75, wherein the secreted ColoUp2 polypeptide is produced by the expression of a nucleic acid having the sequence of SEQ ID No: 5.

78. The method of claim 75, wherein the secreted ColoUp2 polypeptide is produced by the expression of a nucleic acid sequence that is at least 98-99% identical to the nucleic acid sequence of SEQ ID No: 5.

79. The method of claim 1, wherein the secreted ColoUp2 polypeptide has an amino acid sequence that is at least 98-99% identical to an amino acid sequence selected from among SEQ ID No: 3 and SEQ ID No:21.

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80. The method of claim 75, wherein the secreted ColoUp1 polypeptide is selected from among:

a) a secreted polypeptide produced by the expression of a nucleic acid that is at least 95% identical to the amino acid sequence of SEQ ID No: 4;

b) a secreted polypeptide produced by the expression of a nucleic acid that is a naturally occurring variant of SEQ ID No: 4;

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c) a secreted polypeptide produced by the expression of a nucleic acid that hybridizes under stringent conditions to a nucleic acid sequence of SEQ ID No: 4;

d) a secreted polypeptide having a sequence that is at least 95% identical to the amino acid sequence of SEQ ID No: 1; and

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e) a secreted polypeptide having a sequence that is at least 95% identical to the amino acid sequence of SEQ ID No: 2.

81. The method of claim 75, wherein the secreted ColoUp1 polypeptide is produced by the expression of a nucleic acid having the sequence of SEQ ID No: 4.

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82. The method of claim 75, wherein the secreted ColoUp1 polypeptide is produced by the expression of a nucleic acid sequence that is at least 98-99% identical to the nucleic acid sequence of SEQ ID No: 4.

83. The method of claim 1, wherein the secreted ColoUp1 polypeptide has an amino acid sequence that is at least 98-99% identical to an amino acid sequence selected from among SEQ ID No: 1 and SEQ ID No:2.

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84. The method of claim 75, wherein the biological sample is a blood sample or a fraction derived from blood.

85. The method of claim 84, wherein the biological sample is selected from among: whole blood, blood plasma, and blood serum.

86. The method of claim 75, wherein the biological sample is derived from the inner wall and/or lumen of the intestinal tract.
87. The method of claim 86, wherein the biological sample is a stool sample.
88. The method of claim 75, wherein the biological sample is a urine sample.
- 5 89. The method of claim 75, wherein the polypeptide is detected by an assay that employs an antibody.
90. The method of claim 89, where the assay is selected from among: an immunoprecipitation assay, a Western blot, a radioimmunoassays and an enzyme-linked immunosorbent assay (ELISA).
- 10 91. The method of claim 89, wherein the assay comprises contacting the biological sample with an antibody that interacts with a secreted ColoUp1 polypeptide or a secreted ColoUp2 polypeptide.
92. The method of claim 89, wherein the antibody interacts with an epitope of an amino acid sequence selected from among: SEQ ID No: 1 and SEQ ID No: 2.
- 15 93. The method of claim 89, wherein the antibody interacts with an epitope of the amino acid sequence of SEQ ID No: 3.
94. The method of claim 89, wherein the antibody interacts with an epitope of the amino acid sequence of SEQ ID No: 21.
95. The method of claim 89, wherein the antibody is detectably labeled.
- 20 96. The method of claim 95, wherein the label is selected from the group consisting of an enzyme, a fluorescent substance, a chemiluminescent substance, a chromophore, a radioactive isotope and a complexing agent.
97. The method of claim 75, further comprising determining the amount of at least one secreted ColoUp1 polypeptide and/or at least one ColoUp2 in the biological sample.
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98. The method of claim 75, wherein the amount of at least one secreted ColoUp1 polypeptide and/or at least one secreted ColoUp2 polypeptide in the biological sample is compared to a predetermined standard.

5 99. The method of claim 75, wherein the amount of at least one secreted ColoUp1 polypeptide and/or at least one secreted ColoUp2 polypeptide in the biological sample is compared to the subject's historical baseline.

100. The method of claim 75, wherein the presence of at least one secreted ColoUp1 polypeptide and/or at least one secreted ColoUp2 polypeptide is indicative that the subject is likely to harbor a colon adenoma or a colon cancer.

10 101. The method of claim 75, wherein the presence of at least one secreted ColoUp1 polypeptide and/or at least one secreted ColoUp2 polypeptide aids in determining the therapeutic protocol to be administered to a subject having a colon neoplasia.

102. The method of claim 75, wherein the subject was not previously diagnosed with colon cancer.

15 103. The method of claim 75, wherein the subject has previously received or is currently receiving a therapy for colon cancer, wherein the presence of at least one secreted ColoUp1 polypeptide and/or at least one secreted ColoUp2 polypeptide indicates that the subject is likely to have a relapse or a persistent or progressive colon cancer.

20 104. The method of claim 75, wherein the colon neoplasia is a colon adenoma.

105. The method of claim 75, wherein the colon neoplasia is colon cancer.

106. The method of claim 75, wherein the colon neoplasia is metastatic colon cancer.

25 107. The method of claim 75, comprising detecting at least one secreted ColoUp1 polypeptide and at least one secreted ColoUp2 polypeptide in the biological sample.

108. A kit for detecting one or more molecular markers of colon neoplasia in a biological sample, comprising:

- a) an antibody which interacts with an epitope of a secreted ColoUp1 polypeptide or a secreted ColoUp2 polypeptide; and
- b) instructions for use.

109. The kit of claim 108, wherein the antibody interacts with an epitope of a polypeptide selected from among: the polypeptide of SEQ ID No:1, the polypeptide of SEQ ID No:2, the polypeptide of SEQ ID No:3 and the polypeptide of SEQ ID No:21.

110. The kit of claim 108, wherein the antibody is detectably labeled.

111. A purified polypeptide consisting essentially of an amino acid sequence that is at least 95% identical to the sequence of SEQ ID No: 21.

112. The purified polypeptide of claim 111, wherein the purified polypeptide consists essentially of an amino acid sequence that is at least 98-99% identical to the sequence of SEQ ID No: 21.

113. The purified polypeptide of claim 111, wherein the purified polypeptide consists essentially of the amino acid sequence of SEQ ID No: 21.

114. A fusion protein comprising a first polypeptide domain and a second polypeptide domain, wherein the first polypeptide domain consists essentially of an amino acid sequence that is at least 95% identical to an amino acid sequence of SEQ ID No. 21.

115. The fusion protein of claim 114, wherein the second polypeptide domain is a domain selected from the group consisting of: a detection domain, a purification domain and an antigenic domain.

116. An antibody that binds specifically to a ColoUp2 polypeptide consisting essentially of the amino acid sequence of SEQ ID No: 21.

117. The antibody of claim 116, wherein the antibody binds the ColoUp2 polypeptide with a dissociation constant of less than  $10^{-6}$ M.

118. The antibody of claim 116, wherein the antibody is a monoclonal antibody.

5 119. The antibody of claim 116, wherein the antibody is effective for detecting the ColoUp2 polypeptide in a blood sample.

120. The antibody of claim 116, wherein the antibody is effective for detecting the ColoUp2 polypeptide in a sample comprising cells from a colon neoplasia.

121. A method for generating a monoclonal antibody of claim 118, the method comprising:

10 (a) administering to a mouse an amount of an immunogenic composition comprising the ColoUp2 polypeptide effective to stimulate a detectable immune response;

15 (b) obtaining antibody-producing cells from the mouse and fusing the antibody-producing cells with myeloma cells to obtain antibody-producing hybridomas;

(c) testing the antibody-producing hybridomas to identify a preferred hybridoma, wherein the preferred hybridoma is a hybridoma that produces a monoclonal antibody that binds specifically to the ColoUp2 polypeptide;

20 (d) culturing the preferred hybridoma cell culture that produces the monoclonal antibody that binds specifically to the ColoUp2 polypeptide; and

(e) obtaining the monoclonal antibody that binds specifically to the ColoUp2 polypeptide from the cell culture.

122. The method of claim 121, wherein testing the antibody-producing hybridomas comprises testing whether the antibody-producing hybridomas produce an antibody that binds to the ColoUp2 polypeptide in an assay selected from the group consisting of: an enzyme-linked immunosorbent assay, a Bia-core assay and an immunoprecipitation assay.

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